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10/723,374	11/25/2003	Mel Kronick	10031014-1	8009

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EXAMINER	
CALAMITA, HEATHER	
ART UNIT	**PAPER NUMBER**
1637	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

IPOPS.LEGAL@agilent.com

Office Action Summary	Application No.	Applicant(s)	
	10/723,374	KRONICK ET AL.	
	Examiner	Art Unit	
	Heather G. Calamita, Ph.D.	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 October 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-42* is/are pending in the application.

4a) Of the above claim(s) *11 and 17-35* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10, 12-16 and 36-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments, and/or Claims

1. Claims 1-42 are currently pending. Claims 11, 17-35 are withdrawn as being directed to non-elected subject matter. Claims 1-10, 12-16 and 36-42 are currently under examination. All arguments have been fully considered and thoroughly reviewed, but are deemed not persuasive for the reasons that follow. Any objections and rejections not reiterated below are hereby withdrawn.

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1-10 and 12-16 are rejected under 35 U.S.C. 102(a) as being anticipated by Lappin et al. (Journal of Molecular Diagnostics, 2001).

With regard to claim 1, Lappin et al. teach a method of producing a biopolymeric array comprising

determining an anticipated abundance of a target in a sample for which said array is designed to assay (see p. 186, where Lappin discloses determining the concentration of the probes based on hybridizing with a test labeled target nucleic acid. The concentrations of the probes are varied between 1, 3.3, 5, 10, 20, 50 and 100 μM);

identifying a number of copies of a first probe for said first target wherein said identified number of copies is dependent on said determined anticipated abundance (see p. 186, where Lappin discloses the signal intensity is proportional to probe concentration and chooses the

specific concentration of 10 μM to optimize the signal to noise ratio. This choice of 10 μM necessarily identifies the number copies of the probe for the test target); and

immobilizing at least a first population of said number of copies of a first probe for said first target to a surface of a solid support to produce said biopolymetric array (see p. 186, where Lappin discloses experiments were carried out which were intended to optimize signal strength for each probe and then refers to Figures 2 and 6, where the optimum concentration for each probe, once determined was used).

With regard to claim 6, Lappin et al. teach the number of probe copies of said at least first population is chosen so as to provide a particular signal to noise ratio for an array assay using said biopolymeric array (see p. 186, where Lappin discloses the signal intensity is proportional to probe concentration and chooses the specific concentration of 10 μM to optimize the signal to noise ratio. This choice of 10 μM necessarily identifies the number copies of the probe for the test target).

With regard to claim 7, Lappin et al. teach performing a first assay with said sample to determine said at least anticipated abundance of said target (see p. 186, where Lappin discloses experiments were carried out which were intended to optimize signal strength for each probe and then refers to Figures 2 and 6, where the optimum concentration for each probe, once determined was used).

With regard to claim 8, Lappin et al. teach the first assay is performed with an array (see p. 186, Figure 6, where Lappin discloses a reverse dot blot. Applicants have not specifically defined the term "microarray" in the specification therefore a microarry is broadly interpreted as a solid support having oligonucleotide probes attached to it. The reverse dot blot of Lappin therefore meets the limitation of microarray).

With regard to claim 9, Lappin et al. teach the array is a genome-wide array (see p. 178 col. 2 under materials and methods to p. 179 col. 1, where genomic DNA is used to make the probes).

With regard to claim 10, Lappin et al. teach the probe copies are nucleic acids (see p. 186 Figure 5 and legend).

Claims 12-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lappin et al. (Journal of Molecular Diagnostics, 2001) in view of Rothberg et al. (USPN 6,355,423).

With regard to claim 12, Lappin et al. teach. the method further comprises

determining an anticipated abundance of a second target in a sample for which said array is designed to assay (see p. 186 where Lappin discloses determining the concentration of the probes based on hybridizing with a test labeled target nucleic acid. The concentrations of the probes are varied between 1, 3.3, 5, 10, 20, 50 and 100 μM and p. 186, where Lappin discloses experiments were carried out which were intended to optimize signal strength for each probe and then refers to Figures 2 and 6, where the optimum concentration for each of the multiple probes, once determined was used);

identifying a number of copies of a second probe for said second target wherein said identified number of copies is dependent on said determined anticipated abundance (see p. 186, where Lappin discloses the signal intensity is proportional to probe concentration and chooses the specific concentration of 10 μM to optimize the signal to noise ratio. This choice of 10 μM necessarily identifies the number copies of the probe for the test target and Lappin further teaches this was done for each probe); and

immobilizing at least a second population of said number of copies of a second probe for said second target to a surface of a solid support to produce said biopolymetric array (see p. 186, where Lappin discloses experiments were carried out which were intended to optimize signal

strength for each probe and then refers to Figures 2 and 6, where the optimum concentration for each of the multiple probes, once determined was used).

With regard to claim 13, Lappin et al. teach the first target is suspected of being present in a higher abundance than said second target in the sample and the number of probe copies of the first population is less than the number of probe copies in the second population (see p. 186 where Lappin discloses determining the concentration of the probes based on hybridizing with a test labeled target nucleic acid. The concentrations of the probes are varied between 1, 3.3, 5, 10, 20, 50 and 100 μM and p. 186, where Lappin discloses experiments were carried out which were intended to optimize signal strength for each probe and then refers to Figures 2 and 6, where the optimum concentration for each of the multiple probes, once determined was used);

With regard to claim 14, Lappin et al. teach the first target is suspected of bein gpresent in a higher abundance than the second target in the sample and the first population and the second population comprise a density where the density of the first population is less than the density of the second population (see p. 186 where Lappin discloses determining the concentration of the probes based on hybridizing with a test labeled target nucleic acid. The concentrations of the probes are varied between 1, 3.3, 5, 10, 20, 50 and 100 μM and p. 186, where Lappin discloses experiments were carried out which were intended to optimize signal strength for each probe and then refers to Figures 2 and 6, where the optimum concentration for each of the multiple probes, once determined was used)

With regard to claims 15 and 16, Lappin et al. teach a method of preparing a biopolymeric array, said method comprising:

(a) determining the relative abundance of targets in a sample type for which said array is desired to be used (see p. 186, where Lappin discloses determining the concentration of the probes based on hybridizing with a test labeled target nucleic acid. The concentrations of the probes are varied between 1, 3.3, 5, 10, 20, 50 and 100 μM); and

(b) immobilizing populations of different probes for respective targets at relative numbers wherein said relative numbers are chosen based on said determined relative abundance of said targets (see p. 186, where Lappin discloses experiments were carried out which were intended to optimize signal strength for each probe and then refers to Figures 2 and 6, where the optimum concentration for each probe, once determined was used).

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 2-5, and 36-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lappin et al. (Journal of Molecular Diagnostics, 2001) in view of Rothberg et al. (USPN 6,355,423).

The teachings of Lappin are presented above.

With regard to claim 3, Lappin et al. teach at least first population is present in at least two replicate features (see p. 186, where Lappin discloses 7 replicate features).

Lappin does not teach all of the limitations of the clams.

With regard to claim 2, Rothberg et al. teach at least first population is present in at least one feature at a probe density that is in the range of about .001 pmoles/mm^2 to about 10 pmoles/mm^2 (see col. 54 line 14, where Rothberg discloses 0.3 pmoles/mm^2).

With regard to claim 4, Rothberg et al. teach each of said replicate features comprises probes at a density that ranges from about .001 pmoles/mm^2 to about 10 pmoles/mm^2 (see col. 54 line 14, where Rothberg discloses 0.3 pmoles/mm^2).

With regard to claim 5, Rothberg et al. teach the number of probe copies of said at least first population ranges from about 6 x 10^4 probes/feature to about 6 x 10^{12} probes/feature (see col. 57 line 38, where Rothberg discloses 10^6 sequences/cm^2 in cell sizes of 5-10 μm).

With regard to claim 36, Rothberg et al. teach the biopolymeric array has a feature density of about 10 or more on an area of about 10 cm^2 or less (see col. 57 line 38, where Rothberg discloses 10^6 sequences/cm^2 in cell sizes of 5-10 μm).

With regard to claim 37, Rothberg et al. teach the biopolymeric array has a feature density of about 100 or more on an area of about 10 cm^2 or less (see col. 57 line 38, where Rothberg discloses 10^6 sequences/cm^2 in cell sizes of 5-10 μm).

With regard to claim 38, Rothberg et al. teach the biopolymeric array has a feature density of about 1000 or more on an area of about 10 cm^2 or less (see col. 57 line 38, where Rothberg discloses 10^6 sequences/cm^2 in cell sizes of 5-10 μm).

With regard to claim 39, Rothberg et al. teach the biopolymeric array has a feature density of about 10000 or more on an area of about 10 cm^2 or less (see col. 57 line 38, where Rothberg discloses 10^6 sequences/cm^2 in cell sizes of 5-10 μm).

With regard to claim 40, Rothberg et al. teach the biopolymeric array has features ranging in width from about 5.0 to about 500 μm (see col. 57 line 38, where Rothberg discloses a cell size of 5-10 μm).

With regard to claim 41, Rothberg et al. teach the biopolymeric array has features rangining in width from about 10 to about 200 μm (see col. 57 line 38, where Rothberg discloses a cell size of 5-10 μm).

One of ordinary skill in the art at the time the invention was made would have been motivated to apply the method of making an array as disclosed by Lappin with the feature densities and size as disclosed by Rothberg in order to produce an array for high throughput analysis of samples while reducing the signal to noise ratio. Rothberg teaches feature densities and sizes on an array allow for analysis of multiple samples and Lappin teaches a optimizing probe concentration to improve the signal to noise ratio of target analysis. It would have been prima facie obvious to apply the method of making an array as disclosed by Lappin with the feature densities and size as disclosed by Rothberg in order to produce an array for high throughput analysis of samples while reducing the signal to noise ratio.

With respect to claim 42, while Rothberg does not expressly teach the feature width of 50 μm to 150 μm, Rothberg does teach a variety of ranges for feature size and density. These values are results based parameters, therefore one of skill in the art would know to adjust the feature size and density in order to optimize the resulting array for target analysis. Additionally, differences in time, concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

Response to Arguments

4. Applicants' arguments filed October 10, 2007, have been fully considered but they are not persuasive.

Applicants argue beginning at the bottom of p. 8 of the response that while Lappin et al. perform a titration experiment in which probes of different concentration are hybridized with a labeled target, Lappin et al. do not do so in order to anticipated the abundance of the target to which that probe binds. This argument is not persuasive because Lappin et al. do anticipate the

abundance of the target to which the probe binds. Lappin et al. do this when Lappin et al. determine the concentration of the probes based on hybridizing with a test labeled target nucleic acid. The abundance of the target is anticipated when Lappin et al. choose the various concentrations of the probes. Additionally, Applicants argue that Lappin et al. perform the titration experiment in order to optimize the probe concentration for physical variation in the probes themselves. This argument is not persuasive because the reasoning behind why Lappin et al. determine an anticipated abundance of a target in a sample is irrelevant. The only relevant issue is that Lappin et al. do determine an anticipated abundance of a target in a sample.

Furthermore, Applicants argue Lappin et al. do not meet the limitation of "identifying a number of copies of a first probe for said first target wherein said identified number of copies is dependent on said determined anticipated abundance." This argument is not persuasive because as explained in the rejection above Lappin et al. do perform this step. Lappin et al. at p. 186, disclose the signal intensity is proportional to probe concentration and chooses the specific concentration of 10 μM to optimize the signal to noise ratio. This choice of 10 μM necessarily identifies the number copies of the probe for the test target.

Applicants arguments with respect to the 103 (a) rejection are moot in view of the further explanation of the application of Lappin et al.

Summary

5. No claims were allowable.

Conclusion

6. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Correspondence

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Heather G. Calamita whose telephone number is 571.272.2876 and whose e-mail address is heather.calamita@uspto.gov. However, the office cannot guarantee security through the e-mail system nor should official papers be transmitted through this route. The examiner can normally be reached on Monday through Thursday, 7:00 AM to 5:30 PM.

If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Gary Benzion can be reached at 571.272.0782.

Papers related to this application may be faxed to Group 1637 via the PTO Fax Center using the fax number 571.273.8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to 571.272.0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For more information about the PAIR system, see http://pair-direct.uspto.gov.

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